

A genuine attempt seems to have been made to involve all who should or might want to be involved. The result was something like a national town meeting with all the various interests presenting their views on more or less equal footing. The wide spectrum of opinions, some informed and some probably not so well informed, is candidly revealed. Few if any clear directions or recommendations emerged, and it is to be hoped that our political and bureaucratic leadership takes heed and proceeds cautiously.

In a way this approach seems like a breath of fresh air. Those most concerned and interested in this complex problem were being asked rather than being told by government, and the response has the ring of truth. It is possible that a first step has been taken toward solving a major social problem by seeking something approaching a national consensus as opposed to arbitrary legislative fiat or perhaps an imposition of the will of a determined minority. In this exercise one can see the germ of a new more democratic and more participatory approach to solving some of the more difficult social and economic problems of modern America, an approach that will involve all those who should probably be involved in decision making and one that is in the tradition of true participatory democracy which is one of our nation's great heritages. It is to be hoped that the proponents of this approach will not be discouraged by the lack of clear direction or recommendation for NHI at this time. This is simply the way it is. But this outreach effort can be viewed optimistically as an essential first move toward a consensus that will truly reflect the will of the people on this important matter. —MSMW

## REFERENCE

1. National Health Insurance National Outreach Report. U.S. Department of Health, Education, and Welfare, Dec 1977. U.S. Government Printing Office 1978—793—675/158.

## Patent Ductus Arteriosus

THAT A PERSISTENTLY patent ductus arteriosus can produce problems in preterm infants is one of the few clearly established facts in the field. Although complete data are not yet available, the incidence of prematurity is about 15 per 1,000 live births and of these infants about half (8 per 1,000 live births) have a patent ductus arteriosus. The recognition, significance and management of a patent ductus arteriosus are still topics of vigorous debate among neonatologists and pediatric cardiologists. The Specialty Conference in this issue has presented some of the specific views of

the group in San Diego. These views, and some of the concepts presented, do not necessarily agree with those of others working in the same field; this points out the lack of agreement and standardization that exists. These authors have touched on a few of the questions that are currently posed, but unfortunately have not been able to come up with any new clear answers or unifying recommendations. They also have not touched on several very important topics. This failure is not completely for lack of attempt at illuminating the problem, but rather reflects our sadly incomplete understanding of the physiology and pathophysiology of the ductus arteriosus.

It is unfortunate that Dr. Gluck feels that pediatric cardiologists are not an integral part of the overall care of small preterm infants in the intensive care nurseries but rather should be invited only in a consultant role. This is understood when one considers the high incidence of patent ductus arteriosus and that the major advances in diagnosis and management of infants with this disorder come from cardiologists. Even more in keeping with a tandem approach to management of all preterm infants is the not infrequent occurrence of the very subtle signs of a patent ductus arteriosus (and occasionally no signs) as described. These may well require the early use of noninvasive techniques, such as echocardiography, as well as possible invasive techniques, such as retrograde aortography. These both require the services of pediatric cardiologists.

Although important, recognition of the presence of a patent ductus arteriosus with either obvious or subtle signs is not as critical as recognition of the significance of the hemodynamic alterations produced by the left-to-right shunt through the patent ductus arteriosus. Duration and volume of murmurs are notoriously misleading, pulse volume and pulse pressure are frequently increased in normal premature infants, and many of the clinical signs typical of patent ductus arteriosus in older children are not present in premature infants. Echocardiographic assessment of left atrial size as a reflection of shunt magnitude has been a valuable addition to management. As with all individual components of diagnosis, however, an increase in left atrial size can be easily misread or misinterpreted. Changes in blood volume without a shunt could well affect left atrial size. Likewise, variations in ventilator pressures affect the measured left atrial size. An increased left atrial dimension, therefore, does not always mean a patent

ductus arteriosus and conversely a normal left atrial dimension can well be found in the presence of a large shunt.

Because of some of these shortcomings, Dr. Higgins has attempted to introduce a different approach to the assessment of the magnitude of left-to-right shunt and the effects thereof. The data of sequential changes in heart size and pulmonary vascularity are interesting and point out the dynamic nature of the condition and the fallibility of relying on a single observation as an index of severity. In a significant proportion of infants, however, increasing cardiothoracic ratios are not seen and, in the hands of many radiologists and pediatric cardiologists, the degree of plethora in the face of intrinsic pulmonary disease cannot be read with accuracy as he suggests. No doubt the techniques described can and will be refined further.

Once again we must stress that no single clinical or other investigation stands on its own. The integration of both x-ray and echocardiographic evaluation with clinical assessment is mandatory.

Animal experimentation has established clearly that inhibition of prostaglandin synthesis by such pharmacologic agents as indomethacin produces constriction of the ductus arteriosus of fetuses and newborns. Application of this principle to the clinical management of preterm infants with persistently patent ductus arteriosus is still a subject of some controversy. Does indomethacin in fact have a high success rate in closing or constricting the ductus arteriosus sufficiently to reverse heart failure in these infants? The present series, as well as our own, indicates that this is in fact so; other investigators, however, have reported a somewhat lower success rate.<sup>1</sup> If nearly complete success is not assured, are the potentially harmful side effects worth risking? Are these potential side effects in fact a real problem? Are the effects on urine production invariable and what are they due to? Most important, is the transient depression of renal function associated with subsequent permanent damage to the kidney? Conversely, is indomethacin in fact safer than the drugs currently used in the management of congestive heart failure? Diuretic agents, used with impunity, have been studied as little as indomethacin in preterm infants.

All of these, and many other questions, require answering before we can safely recommend indomethacin as the therapy of choice for all infants under all conditions. Until then, carefully con-

trolled evaluation of the efficacy and the effects, both short-term and long-term, must continue.

Dr. Friedman has addressed several of these problems; specifically, the effects of indomethacin on renal function have been investigated in experimental animals. His experimental data on the reduction of renal blood flow are not in agreement with our own, probably because of the measurement techniques used. Our studies with radionuclide labeled microspheres, which measure flow directly, show no change in renal blood flow nor in intrarenal distribution of blood flow.<sup>2</sup> Since prostaglandins affect renal function in many other different ways, we must look to other mechanisms for the reduction in urine volume seen with the clinical usage of this drug. That there is a disturbance of renal function in a high percentage of treated infants is clear; however, this is not an essential side effect of the drug and when it does occur it is only transient. As indicated by Dr. Merritt, long-term follow-up is required and in the few infants so followed no effects were noted.

Will indomethacin turn out to be the drug of choice or will a more selective agent be found? If indomethacin in fact is to be used, what is the appropriate dose? When during the course of the disease should it be given, and when should it be repeated or, in fact, should it be repeated? Little is known about the pharmacokinetics of indomethacin in preterm infants but it is likely that the half-life is considerably longer than that in the adult. Is the well-known reduction of platelet aggregation associated with an increased incidence of hemorrhage in the preterm infant? Does indomethacin have a significant effect on other organs that we are not able to detect readily? What is the interrelationship of the inhibition of prostaglandin synthesis and the sympathetic nervous system, particularly in relationship to the control of systemic vascular beds? This latter question is of great significance since these are stressed infants in whom the sympathetic nervous system is likely to be highly activated. It is clear that only well-controlled, large scale studies will provide answers to these questions.

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2. Benson D, Lister G, Heymann MA, et al: Effects of indomethacin on renal function in newborn lambs. *Circulation* 56:192, 1977 (abstr)